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Research article

Dexmedetomidine–Oxycodone combination for conscious sedation during colonoscopy in obese patients: A randomized controlled trial

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ABSTRACT

Background: Obesity is a risk factor for sedation-related respiratory depression during colonoscopy. In a colonoscopy, propofol is frequently used because of its strong sedative and hypnotic properties. However, propofol is associated with marked respiratory depression. The objective of this trial was to investigate the effectiveness and safety of dexmedetomidine plus oxycodone for conscious sedation during colonoscopy in obese patients.

Methods: A total of 120 patients had colonoscopies, and they were divided into two groups at random: Dexmedetomidine and oxycodone were used to sedate group Dex + oxy; while group Pro + oxy received anesthesia with propofol plus oxycodone. Parameters including blood pressure, heart rate, respiration, blood oxygen saturation, injection pain, and recovery time were recorded for both groups.

Results: The incidence of hypoxemia was significantly reduced in group Dex + oxy compared with group Pro + oxy (4.9% *vs* 20.3%, $P = 0.011$). Blood pressure was lower, and heart rate was higher in group Pro + oxy compared with group Dex + oxy ($P < 0.05$). In addition, group Dex + oxy showed a significantly shorter caecal insertion time, recovery time to orientation, and recovery time to walking than group Pro + oxy ($P < 0.05$). Endoscopist satisfaction scores were significantly higher in group Dex + oxy compared with group Pro + oxy ($P = 0.042$).

Conclusion: For obese patients, dexmedetomidine plus oxycodone effectively sedate them with few adverse effects, while also reducing colonoscopy operation difficulty by allowing obese patients to reposition. Thus, dexmedetomidine plus oxycodone could be used safely as a conscious sedation method for colonoscopy in obese patients.

Trial registration: The protocol was registered at www.chictr.org.cn (ChiCTR1800017283, July 21, 2018).

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1. Introduction

The prevalence of obesity in adults has increased rapidly in China over several decades. An estimated 85 million adults aged 18–69 years in China were obese in 2018 [1,2]. Several illnesses, including colorectal cancer, have been associated with obesity and being overweight (defined as having a body mass index [BMI] $\geq$ 25 kg/m^2) [3]. Early colonoscopy is an effective way to prevent morbidity and mortality from colorectal cancer [4]. However, colonoscopy and sedation can be challenging in obese patients.

Evidence suggests that a raised BMI can lead to difficulties in achieving caecal intubation and prolongs caecal intubation times during colonoscopy [5,6]. Additionally, obesity is an independent predictor of inadequate bowel preparation during colonoscopy [7], which indirectly contributes to difficult caecal intubation. Moreover, during colonoscopy in obese patients, repositioning and abdominal compression are often performed to facilitate the advancement of the endoscope [8], and sedation make it more challenging to move an obese patient.

Although helpful for identifying and treating colon diseases, colonoscopy can make some patients uncomfortable, including by causing stomach pain, anxiety, and fear [9,10]. With advancements in anesthesia, painless colonoscopy has become a reality. Propofol is the most common intravenous anesthetic used during a painless colonoscopy [11]. It has a short half-life and rapidly induces anesthesia [12]. However, it significantly suppresses both respiratory and circulatory systems with poor analgesic effects [13,14]. This is a major challenge for the anesthetist.

Dexmedetomidine is a selective α2 adrenoreceptor agonist that provides anxiolysis and sedation with minimal respiratory depression [15–18]. Conscious sedation with dexmedetomidine allows patients to be awakened and repositioned during colonoscopy [18]. Additionally, the kappa-opioid agonist oxycodone, which targets visceral pain more effectively than dexmedetomidine [19,20], can be used in conjunction with it during colonoscopy.

The study aims to investigate the sedation effects of dexmedetomidine plus oxycodone alongside the effects on respiration and colonoscopy operation, and to seek a more suitable sedation method for colonoscopy in obese patients.

2. Methods

2.1. Participants

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was registered at www.chictr.org.cn (ChiCTR1800017283). This study was approved by the Ethics Committee of Suqian People's Hospital and Xuzhou Central Hospital. Participants were recruited from July 2018 to October 2020. All patients who underwent colonic endoscopy provided written informed consent. Inclusion criteria: American Society of Anesthesiologists (ASA) class I or II; body mass index (BMI) 30 to 35; age between 30 and 60 years; and elective colonoscopy. Exclusion criteria: difficult airway (the presence of predictors of difficult mask ventilation and difficult intubation, such as altered dentition, Ankylosing Spondylitis, Pierre-Robin syndrome, Mallampati scores $\geq$ III et al.); grade 3 hypertension; coronary heart disease; bradycardia (heart rate falls below 60); neurological or mental illness; decompensated liver or kidney disease; hypersensitivity reactions to any of administered drugs, pregnancy, contraindications to the use of dexmedetomidine (treatment with a beta blocker or digoxin), alcoholism (drink at least 3 standard drinks a day or 5 standard drinks at least once a week). The patients were randomly assigned into one of two groups (allocation ratio was 1:1) by computer-generated random numbers before the endoscopy procedure. Group Dex + oxy received dexmedetomidine plus oxycodone, and group Pro + oxy received anesthesia with propofol plus oxycodone.

2.2. Anesthesia method and outcome measure

All participants were limited to a clear liquid diet for dinner the day before the colonoscopy. The polyethylene glycol electrolyte was to be taken by the patients at 8 or 9 o'clock that evening with 1 L of water. On the next day, they were encouraged to follow the same regimen 5–6 h before the colonoscopy. Once the patient was in the procedure room, supplementary oxygen was administered (2 L/min) via a nasal cannula. Blood pressure, heart rate, respiration, blood oxygen saturation, and STOP-BANG (snoring, tiredness, observed apnea, blood pressure, body mass index, age, neck size, gender) score were all monitored, as well as pain from the drug injection. The STOP-BANG questionnaire was developed in response to the need for a valid, user-friendly method to assess irregular breathing during sleep. Group Dex + oxy received 0.1 mg/kg intravenous oxycodone hydrochloride and 0.6 μg/kg dexmedetomidine in 10 min followed by a continuous pump infusion of 0.2 μg/kg/h dexmedetomidine. Colonoscopy began 10 min after the administration of dexmedetomidine in Group Dex + oxy. Group Pro + oxy received 0.1 mg/kg intravenous oxycodone hydrochloride and 1 mg/kg intravenous propofol. If the patient began to move, additional propofol doses (20–30 mg) were given. Colonoscopy began once the eyelash reflex disappeared in Group Pro + oxy.

Throughout the procedure, heart rate (HR), respiration, and pulse oxygen saturation (SpO2) were continuously monitored. The respiratory rate was recorded using the end-tidal CO_2 waveform. Hypoxemia was defined as $SpO_2 < 90\%$. Blood pressure was monitored every 2 min. Hypotension was defined as mean arterial pressure (MAP) < 70 mmHg. Bradycardia was defined as HR < 60 beats/minute. MAP, SpO_2, and HR were recorded in both groups before sedation or anesthesia (T1), when the endoscope was inserted into the anus (T2), when the endoscope reached the splenic flexure (T3), when the endoscope reached the hepatic flexure (T4) when the endoscope reached the ileocaecal area (T5) and at the end of the procedure (T6).

When SpO2 was less than 90% or when the end-tidal CO_2 waveform vanished, airway maneuvers (jaw thrust, chin lift), and bag-

mask ventilation, would be used. Ephedrine 3 mg was administered when systolic blood pressure (SBP) was under 80 mmHg or had a greater than 30% reduction from baseline measurement. The procedure was stopped when the patient's heart rate dropped to 50 beats per minute, and atropine 0.3–0.5 mg was injected intravenously. Only after reaching the ileocaecal region were biopsies or polypectomies carried out.

The recovery time was measured from the end of the procedure to patients reaching a Ramsay Sedation Scale (RSS) score of 2. The discharge time was also recorded from the end of the endoscopy to achieving a Steward Recovery Score (SRS) of 6. Patients were asked about drug injection pain and any other discomfort. The results of surveys of endoscopists and patients' satisfaction were calculated (between 1 and 4) [21]. Blinding was difficult in this study. Endoscopists, anesthetists, and patients were unblinded.

2.3. Statistical analysis

Previous studies showed a 20–30% hypoxemia rate amongst all-comers under propofol-based monitored anesthesia, without endotracheal intubation, during endoscopic procedures [22,23]. In obese patients receiving dexmedetomidine plus oxycodone anesthesia for colonoscopy, our institutional experience revealed a hypoxemia rate of less than 5%. We assumed a 25% hypoxemia rate in obese patients sedated with propofol plus oxycodone. Hence, to detect a reduction in hypoxemia rate from 25% to 5%, 100 patients would be needed to achieve a statistical power of 80% ($\alpha = 0.05$, $\beta = 0.2$). To account for potential dropouts, we planned to include 120 patients.

IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Continuous and categorical data were presented as mean ± standard deviation (SD) and n (%), respectively. Independent-sample *t*-test and Chi-square/Fisher's exact tests were used to analyze continuous and categorical data, respectively. The threshold for statistical significance was set at 0.05.

3. Results

3.1. Patient characteristics

A total of 138 patients were enrolled in the study, 18 of whom had to be removed because of inadequate intestinal prepping. The remaining 120 patients completed colonoscopy under sedation with oxycodone hydrochloride plus dexmedetomidine (N = 61) or propofol (N = 59). The flow of patients through the study and detailed reasons for exclusion are provided in Fig. 1. Table 1 summarizes

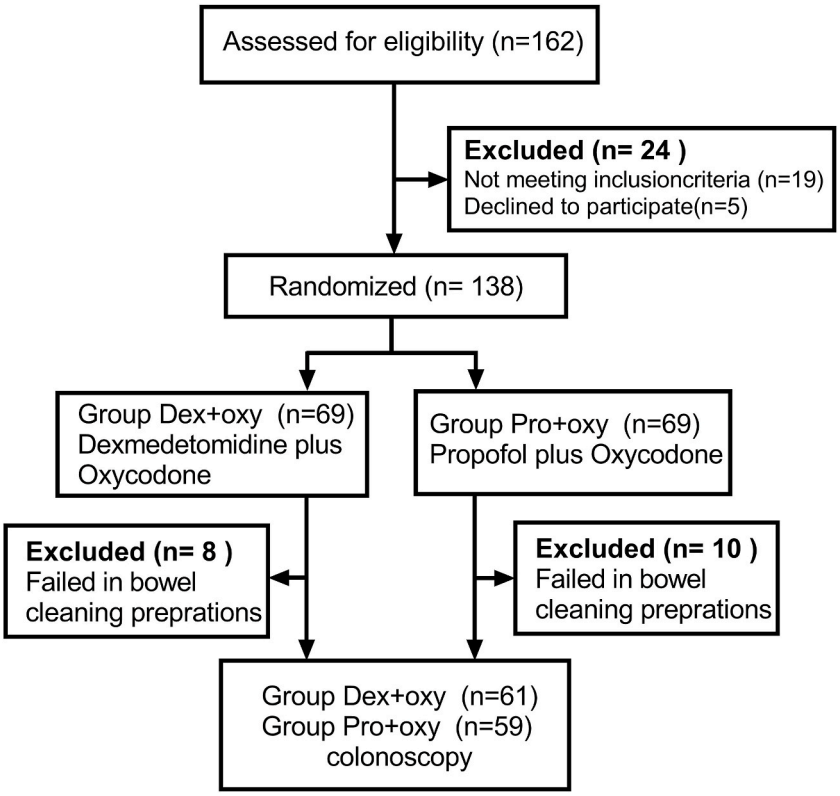

Fig. 1. Enrolment flowchart of patients through the study.

Table 1
Demographic and clinical characteristics.

Admission characteristics	Dex + oxy (N = 61)	Pro + oxy (N = 59)	P value
Age (years)	46.8 ± 6.6	47.2 ± 7.1	0.582
BMI (kg/m^2)	33.2 ± 1.50	33.0 ± 1.53	0.265
Sex (M/F), n	36/25	34/25	0.876
Hypertension, n (%)	10 (16.4%)	9 (15.3%)	0.865
Diabetes mellitus, n (%)	7 (11.5%)	8 (13.5%)	0.730
STOP-BANG score	3.4 ± 1.4	3.3 ± 1.2	0.238
Indications, n (%)			
Screening	28 (45.9%)	24 (40.7%)	0.419
Surveillance	24 (39.3%)	26 (44.1)	0.600
Hematochezia	5 (8.2%)	8 (13.6%)	0.345
Diarrhea	2 (3.3%)	0 (0)	0.496$^{\#}$
Abdominal pain	2 (3.3%)	1 (1.7%)	1.000$^{\#}$
Total drugs used			
Dexmedetomidine (μg)	61.8 ± 11.2	–	–
Propofol (mg)	–	265 ± 93	–
Oxycodone (mg)	10.2 ± 2.1	9.41 ± 1.8	0.212

Dex + oxy, dexmedetomidine + oxycodone; Pro + oxy, propofol + oxycodone; BMI, body mass index; STOP-BANG, snoring, tiredness, observed apnea, blood pressure, body mass index, age, neck size, gend; $^{\#}$ Fisher's exact test; Values are mean ± SD or number (percentages).

the fundamental demographic and clinical characteristics of the two groups.

3.2. Respiration and hemodynamic parameters

Mean arterial pressure (MAP) was reduced in group Pro + oxy compared with group Dex + oxy when the endoscope was inserted into the anus, following induction of anesthesia (T2) ($P < 0.05$) (Fig. 2A). Heart rate was lower in group Deo + oxy compared to group Pro + oxy at four-time points (T2-T6) between the beginning of anesthesia and when the endoscope reached the ileocecal area ($P < 0.05$) (Fig. 2B). At three time points (T2-T4), SpO_2 was reduced in group Pro + oxy compared with group Dex + oxy ($P < 0.05$) (Fig. 2C).

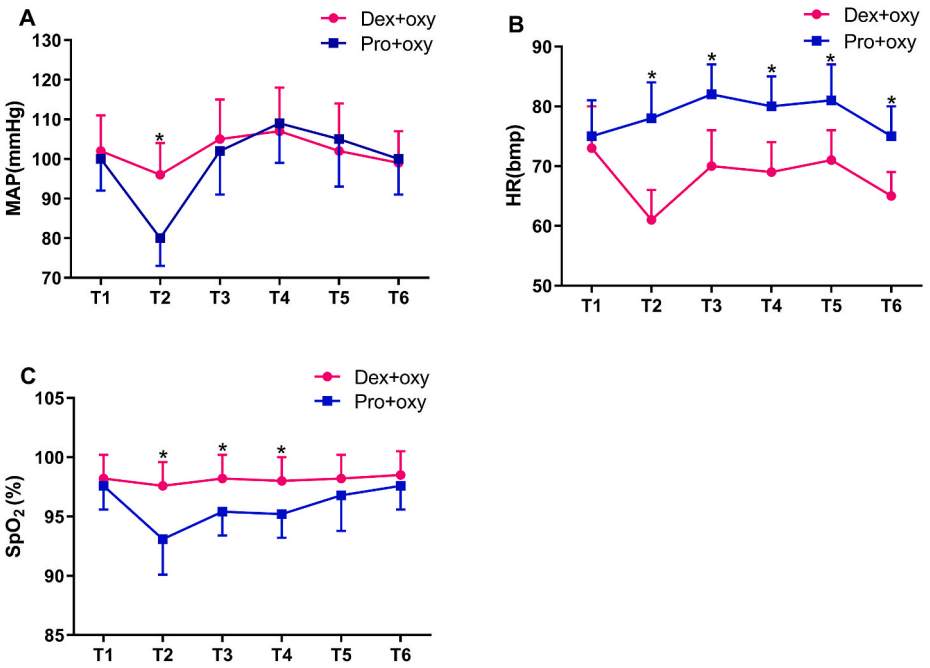

Fig. 2. (**A**)The changes in blood pressure (MAP, mean arterial pressure) in two groups. (**B**) The changes of heart rate (HR) in two groups. (**C**) The changes in pulse oxygen saturation (SpO_2) in two groups. Dex + oxy, dexmedetomidine + oxycodone; Pro + oxy, propofol + oxycodone; *$P < 0.05$ versus group Pro + oxy. T1, before anesthesia; T2, the endoscope inserted into the anus after induction of anesthesia; T3, the endoscope reached the splenic flexure; T4, the endoscope reached the hepatic flexure of the colon; T5, the endoscope reached the ileocecal area; T6, end of endoscopy. Error bars represent standard deviations.

Table 2
Sedation-related adverse events.

	Dex + oxy (N = 61)	Pro + oxy (N = 59)	P value
Injection pain	0 (0%)	16 (27.1%)	<0.001
Hypoxemia	3 (4.9%)	12 (20.3%)	0.011
Hypotension	0 (0%)	8 (13.6%)	0.003[a]
Somatic movement	4 (6.6%)	2 (3.4%)	0.680[a]
Bradycardia	13 (21.3)	7 (11.9)	0.165
Chin lift	6 (9.8%)	12 (20.3%)	0.107
Jaw thrust	1 (1.6%)	9 (15.3%)	0.008[a]
Bag-mask ventilation	0 (0%)	4 (6.8%)	0.055[a]
Nausea and vomiting	3 (4.9%)	2 (3.4%)	1.000[a]
Ephedrine application	0 (0%)	2 (3.4%)	0.240[a]
Atropine application	3 (4.9%)	1 (1.7%)	0.619[a]

[a] Fisher's exact test; Data presented as number (percentages).

Table 3
CIT, recovery and discharge time, satisfaction of patients and operator

	Dex+oxy (N=61)	Pro+oxy (N=59)	P value
CIT, (min)	6.2 ± 3.5	10.2 ± 5.3	0.001
Recovery time, (min)	1.4 ± 0.8	8.5 ± 2.6	<0.001
Discharge time, (min)	9.6 ± 2.8	14.2 ± 5.6	0.012
Satisfaction of patient	3.7 ± 0.4	3.9 ± 0.3	0.653
Satisfaction of operator	3.8 ± 0.2	3.1 ± 0.2	0.042

CIT, caecal insertion time; Data presented as mean ± SD.

3.3. Adverse reactions

When compared to group Dex + oxy, the incidence of hypoxemia, hypotension, and drug injection pain was significantly higher in group Pro + oxy ($P < 0.05$). The number of times airway intervention was required (jaw thrust) in group Dex + oxy was lower than that in group Pro + oxy ($P < 0.05$). (Table 2).

3.4. Secondary outcome

When compared to group Pro + oxy, the recovery and discharge times were significantly shortened in the Dex + oxy group ($P < 0.05$). There were no statistically significant differences between the two groups in terms of patient satisfaction, but endoscopist satisfaction scores were higher in the Dex + oxy group ($P < 0.05$) (Table 3). The caecal insertion time was shorter for patients in group Dex + oxy than patients in group Pro + oxy ($P < 0.05$). The endoscopist did not perform any biopsies or polypectomies before the endoscope reached the ileocecal area.

4. Discussions

This study is the first prospective, randomized controlled trial contrasting anesthesia with propofol plus oxycodone with sedation with dexmedetomidine plus oxycodone during colonoscopy in obese patients. We found that sedation with dexmedetomidine plus oxycodone is associated with a lower incidence of sedation-related adverse events. Furthermore, sedation with dexmedetomidine plus oxycodone facilitated difficult colonoscopies in obese patients due to relatively free body positioning.

Obesity is a risk factor for sedation-related respiratory depression during colonoscopy. The sedative and hypnotic properties of propofol make it a popular choice for colonoscopies. However, propofol is associated with marked respiratory depression, especially for obese patients [24,25]. In our study, sedation with propofol plus oxycodone was associated with a significantly higher incidence of hypoxemia necessitating airway intervention. Dexmedetomidine, a sedative α_2-adrenoceptor agonist that mimics natural sleep in humans, has been widely used to induce anesthesia and sedate patients in intensive care [26–29]. Oxycodone is a dual μ and κ-opioid receptor agonist with good analgesic effects on visceral pain and fewer adverse effects, such as gastrointestinal motility suppression or respiratory depression [30,31]. This study demonstrated that dexmedetomidine plus oxycodone hydrochloride exhibited good sedative effects with little respiratory depression. It should be stressed here that the risk of respiratory depression caused by dexmedetomidine is low but still exists. Therefore, there must be no slackness in monitored anesthesia care.

When a patient is older and has underlying medical conditions, hemodynamic stability is crucial to ensuring their safety during anesthesia [32]. This study showed that dexmedetomidine plus oxycodone hydrochloride caused a slight reduction in heart rate with minimal effects on blood pressure, which has important clinical implications in patients with cardiovascular and cerebrovascular diseases. Hemodynamic stability ensures tissue perfusion of vital organs, such as the heart and brain. Moreover, a slight decrease in heart rate reduces myocardial oxygen consumption, which may protect the myocardium [33–35]. Nevertheless, heart rate monitoring needs to be emphasized. In theory, vagus reflex during colonoscopy may increase the risk for bradycardia under sedation with

dexmedetomidine.

Obese patients present unique challenges during colonoscopy [6,7]. Patients often need to reposition during the procedure to facilitate the advancement of the endoscope. An obese patient who is heavily sedated, however, may be challenging for the endoscopist and support staff to reposition [8,36]. Conscious sedation with dexmedetomidine and oxycodone meant that patients could be awakened and could be repositioned, facilitating difficult colonoscopy, improving patient compliance, and reducing the need for support staff to move the patient. This study revealed that the caecal insertion time was shorter, and endoscopist satisfaction scores were higher when sedated with dexmedetomidine plus oxycodone.

There are limitations to this study. First, a double-blind design could not be used throughout the entire experiment. The endoscopist would observe that some patients might awaken, and although there is an inherent risk of bias toward the intervention group, we hoped to reduce this bias by using a more objective visibility scoring system rather than a subjective report of visibility adequacy by the endoscopist. Second, patients undergoing conscious sedation may remember having the procedure, although, our study demonstrated that conscious sedation does not significantly increase procedure-related discomfort. Third, the depth of sedation in the two groups was different. We don't know if the variation in the incidence of respiratory depression was caused by the drug's pharmacological characteristics or by the degree of sedation. Fourth, both our study and previous research have demonstrated that dexmedetomidine intravenous infusions cause bradycardia [37,38]. Hence, sedation with dexmedetomidine would be contraindicated in patients with bradycardia and those taking drugs affecting cardiac conduction and rate. Finally, fluid and electrolyte imbalance e indeed a concern in bowel preparation. Clinicians should be alert to the risk of diuresis and water-electrolytes when using dexmedetomidine because studies have shown that dexmedetomidine has a potential diuretic effect [39,40]. Future studies should clarify the effects of dexmedetomidine on water-electrolyte balance during colonoscopy.

5. Conclusions

In conclusion, dexmedetomidine and oxycodone exhibit good sedative effects and minimal respiratory depression during conscious sedation for colonoscopy. Patients generally approve of this sedation technique, which does not significantly increase discomfort related to the procedure. For obese patients, sedation with dexmedetomidine plus oxycodone is worthy to be considered.

Author contribution statement

Xinran Wang, Manman Zhang, Han Sun: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Rui Zhang: Performed the experiments.

Yangzi Zhu, Zhen Zhang, Rongxia Shi: Conceived and designed the experiments.

Data availability statement

Data will be made available on request.

Funding information

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Informed consent

All patients participating in the clinical trial provided written informed consent.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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